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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STUCKER, JEFFREY J	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,534	ENSOLI, BARBARA	
	Examiner	Art Unit	
	Jeffrey Stucker	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2004 and 09 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *62,63,65,66,68,69,76,77,79 and 89-139* is/are pending in the application.

4a) Of the above claim(s) *124-126,130-132 and 134* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *62,63,65,66,68,69,76,77,79,89-123,127-129,133 and 135-139* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This Office Action is in response to the RCE filed 9 August 2004 which permitted entry of the amendment filed 9 April 2004. Claims 62, 63, 65, 66, 68, 69, 76, 77, 79, and 89-139 are pending. Newly submitted claims 124-126, 130-132, and 134 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons: The original claims are directed to a wild-type strain whereas the withdrawn claims are directed to various mutant strains with several sequences that are different from the examined wild-type strain.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 124-126, 130-132, and 134 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Therefore, claims 62, 63, 65, 66, 68, 69, 76, 77, 79, and 89-123, 127-129, 133, and 135-139 are examined and rejected.

The rejection of claims 62-72 and 76-88 under 35 U-.S.C. 112, first paragraph, because the specification, while being enabling for inducing an immune response, does not reasonably provide enablement for vaccines for treating or

preventing HIV related disease **is withdrawn** in view of applicant's amendment of "non-aggregated and non-oxidized".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 62, 63, 69, 77, 90, 91, and 96 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear how the characteristic of "purified" (63/77) further limits "isolated" (62/96).

In Claims 69, 90, and 91, it is not clear what is meant by a lyophilized diluent/excipient. If one were to lyophilize the composition of claim 62 which contains an excipient and/or diluent, that would remove the excipient and diluent, which are liquids.

Applicant is reminded of applicant's duty to disclose relevant prior art to the PTO.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 62, 63, 65, 66, 68, 69, 76, 77, 79, 89, 90, 93-94, 106, 107, 115, 120, 128, 129, 133, and 137 are rejected under 35 U.S.C. § 102(b) as being anticipated by Chang et al.

The claimed invention is directed to a Tat protein, fragment thereof or mutant thereof or a combination thereof in a non-aggregated and non-oxidized form with specific characteristics. It is further limited to be in a form suitable for administration by various routes and purified by heparin affinity chromatography, lyophilized form, resuspended in a degassed buffer, a fluid which is serum, plasma, or one or more fractions thereof, and comprises a fragment of Tat. The Tat sequence is a wild-type strain consisting of SEQ ID NO:2.

The claimed limitations and the relevant portions of the reference are set forth below:

a Tat protein, fragment thereof or mutant thereof or a combination thereof in a non-aggregated and non-oxidized form with specific characteristics:

the instant Tat protein appears to be the same protein as disclosed in the reference because it is from the same source and same purification protocol, page 1424 under "Purification of recombinant Tat protein by heparin affinity chromatography" and 1429, top of the first column;

in a form suitable for administration by various routes:

the protein of the reference is administered to rabbits (pg 1424, first column, under "Tat protein and anti-Tat antibody");

purified by heparin affinity chromatography:

top of page 1424, though it should be noted that this does not necessarily limit the structure of the composition;

lyophilized form and resuspended in a degassed buffer:

page 1424, first column, under "Tat protein and anti-Tat antibody";

a fluid which is serum, plasma, or one or more fraction thereof:

page 1424, first column, under "Tat protein and anti-Tat antibody", 0.1% BSA;

wild-type strain consisting of SEQ ID NO:2:

SEQ ID NO:2 is the same Tat sequence from the same viral strain, HIV_{IIIB}, as is used in the reference; see page 1423, under

"Plasmid DNA and transfection of COS-1 cells" which refers to reference No. 18 which uses HIV_{IIIB} as the origin of the Tat protein;

comprises fragment of Tat:

the broad language of "comprises a fragment" reads on the entire protein.

Thus, the claimed invention is anticipated by Chang et al.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 62, 63, 65, 66, 68, 69, 76, 77, 79, 89, 90, 93-94, 106, 107, 112, 115, 120, 128, 129, 133, and 137 are rejected under 35 U.S.C. § 103(a) as obvious over Chang et al. in view of Chengalvala et al. (*Vaccine*, 1999).

The claimed invention is further limited to conjugating a T-helper universal epitope of tetanus toxoid to the Tat protein.

The relevance of Chang et al. is given above.

Chengalvala et al. teach that conjugating the T helper epitope of tetanus toxoid to HBsAg enhances the immunogenicity of the HBsAg. See the entire reference. Note also that the reference teaches on the first column of page 1036 that conjugating the T helper epitope of tetanus toxoid to a B cell epitope peptide from the major surface protein of *P. falciparum* enhanced the antibody response to this peptide by several fold. It would have been obvious to one of ordinary skill in the art at the time the invention was made to conjugate the T cell helper epitope of tetanus toxin of Chengalvala et al. to the Tat protein of Chang et al. One would be motivated to do this in order to enhance the immunogenicity Chang et al.'s Tat protein. Thus, the claimed invention is obvious over Chang et al. in view of Chengalvala et al.

Claims 62, 63, 65, 66, 68, 69, 76, 77, 79, 89, 90, 93-94, 106, 107, 113-115, 118-120, 128, 129, 133, and 135-137 are rejected under 35 U.S.C. § 103(a) as obvious over Chang et al. in view of Heiman et al. (*Nature Med. Vac. Supp.*, 1998).

The claimed invention is further limited to a non-Tat HIV proteins, specifically rev, nef, or gag. The composition can comprise the proteins or comprise the proteins conjugated to Tat.

The relevance of Chang et al. is given above.

The review article by Heiman et al. teach numerous combinations of HIV proteins are known in the art. They specifically reference gag at pages 3-5. It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the protein of Chang et al. with the antigens of Heiman et al. with the expectation of at least an additive effect. It would have been further obvious to one of ordinary skill in the art at the time the invention was made to conjugate the gag protein to Tat protein so as to link the gag immune response with the Tat protein response. Thus, the instantly claimed invention is obvious over Chang et al. in view of Heiman et al.

Claims 62, 63, 65, 66, 68, 69, 76, 77, 79, 89, 90, 93-95, 97, 101-111, 115-117, 120-122, 128, 129, 133, and 137-139, are rejected under 35 U.S.C. § 103(a) as obvious over Chang et al. in view of Vogel et al. (1995).

The claimed invention is further limited to the addition of a cytokine wherein the cytokine can be IL-12. The cytokine may further be conjugated to the Tat protein.

The relevance of Chang et al. is given above.

Vogel et al. teach that IL-2 modulated the immune system through the T cell pathway. See entire reference. It would have been obvious to one of ordinary skill in the art at the time the invention was made to add this cytokine to the composition of Chang et al. with the expectation of favorably modulating the immune system. It would have been further obvious to conjugate the cytokine to the protein so as to link the favorable immune response with the Tat protein.

Vogel et al. teach that alum is a well known and studied adjuvant. As the authors note in the introductory paragraph on page 1, alum is the only adjuvant used in human vaccine licensed in the United States. It would have been obvious to one of ordinary skill in the art at the time the invention was made to add this well known adjuvant to the composition of Chang et al. with the expectation of enhancing the immune reaction to Tat. Thus, the instantly claimed invention is obvious over Chang et al. in view of Vogel et al.

Claims 62, 63, 65, 66, 68, 69, 76, 77, 79, 89, 90, 93-94, 106, 107, 115, 120, 123, 128, 129, 133, and 137 are rejected under 35 U.S.C. § 103(a) as obvious over Chang et al. in view of Hengge et al. (*AIDS*, 1998).

The invention is further limited to the addition of an inhibitor of viral replication to the claimed composition.

The relevance of Chang et al. is given above.

Hengge et al. teach that various viral inhibitor compounds were known in the art, specifically, zidovudine, 3TC, and saquinavir. See the entire reference, specifically, the last paragraph of the first column on page F226. It would have been obvious to one of ordinary skill in the art at the time the invention was made to include the addition of an antiviral composition in the composition to inhibit viral disease. Thus, the instantly claimed invention is obvious over Chang et al. in view of Hengge et al.

Claims 62, 63, 65, 66, 68, 69, 76, 77, 79, 89, 90, 93-94, 99, 106, 107, 115, 120, 128, 129, 133, and 137 are rejected under 35 U.S.C. § 103(a) as obvious over Chang et al. in view of Castignolles et al. (*Vaccine*, 1996).

The invention is further limited to the addition of nanoparticles to the claimed composition.

The relevance of Chang et al. is given above.

Castignolles et al. teach that nanoparticles have immunostimulating properties. See the abstract and the discussion section. It would have been obvious to one of

ordinary skill in the art at the time the invention was made to combine the nanoparticles of Castignolles et al. with the Tat protein of Chang et al. with the expectation of enhancing the immune response to the protein. Thus, the instantly claimed invention is obvious over Chang et al. in view of Castignolles et al.

Claims 62, 63, 65, 66, 68, 69, 76, 77, 79, 89, 90, 93-94, 100, 106, 107, 115, 120, 128, 129, 133, and 137 are rejected under 35 U.S.C. § 103(a) as obvious over Chang et al. in view of Ramshaw et al. (*J. of imm. methods*, abstract only, 1977).

The composition is further limited including autologous erythrocytes in the claimed composition.

The relevance of Chang et al. is given above.

Ramshaw et al. teach that autologous erythrocytes (red blood cells) are efficient at inducing an immune response. It would have been obvious to one of ordinary skill in the art at the time the invention was made to couple the Tat protein of Chang et al. to autologous erythrocytes to efficiently induce an antibody response. Thus, the instant invention is obvious over Chang et al. in view of Ramshaw et al.

No claims are allowed.

Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

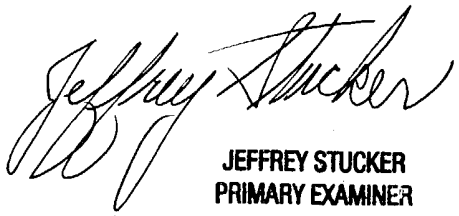
The Group 1600 Official Fax number is: (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Stucker whose telephone number is (571)-272-0911. The examiner can normally be reached Monday to Thursday from 7:00am-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (571)-272-0902.



JEFFREY STUCKER
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